

Glycerol Monooleate

processing

Executive Summary

Glycerol monooleate is a synthetic compound that is considered a monoglyceride. The petitioned purpose is for use as a defoamer, but the substance has a number of food applications, as well as application as an excipient in pharmaceutical products.

The Reviewers recognize that foam is a problem that needs to be addressed in organic food processing. The Reviewers were divided on whether to add the substance to the National List. One reviewer had concerns about health impacts based on a review of recent literature, while another reviewer felt that the health concerns were not sufficient to restrict use in view of a demonstrated need for defoaming agents. No Reviewer supported listing the product without annotations; each proposed to limit use in organic food processing. One suggested an annotation consistent with the current limitation on glycerin, another sought to limit use only to those products labeled as 'Made With Organic [specified ingredients],' and the third suggested prohibition without annotation.

Identification

Chemical Name:

glycerol monooleate

Other Names:

9-Octadecenoic acid (Z)-, monester with 1,2,3-propanetriol; glycerol monoleate; glyceryl monooleate; glyceryl oleate; glyceryl oleate; glycerol oleate; GM; GMO; 1-Oleoyl-sn-glycerol; monoolein.

Trade Names:

Aldo MO FG; Atsurf 594; Atsurf 595, Atsurf 595K, Atsurf 596, Atsurf 596K, Lumulse GMO FGK; Capmul GMO, Cithrol GMO N/E; Drewmulse 200; Dur-Em

GMO; Emrite 6008; GMO 0041; Hodag GMO; Hodag GMO-D; Mazol 300 K; Mazol GMO; Mazol GMO k; Monomuls 90-O18; Nikkol MGO; Pationic 1061, Pationic 1064; Pationic 1074 (Ash and Ash, 1995).

CAS Numbers:

25496-72-4 (glycerol monooleate)
111-03-5 (glycerol oleate)
37220-82-9 (glycerol mono/dioleate)

Other Codes:

EINECS: 203-827-7; 253-407-2
IFN: 8-15-844

Summary of TAP Reviewer Analysis¹

95% organic

Synthetic / Nonsynthetic:	Allowed or Prohibited:	Suggested Annotation:
<i>Synthetic (3)</i>	<i>Prohibited (2)</i> <i>Allowed (1)</i>	<i>Prohibited without annotations. (2)</i> <i>Allowed provided that the glycerine used in the production of glycerol monooleate must be made by hydrolysis of fats and oils. (1)</i>

Made with Organic (70%+) [specified ingredients]

Synthetic / Nonsynthetic:	Allowed or Prohibited:	Suggested Annotation:
<i>Synthetic (3)</i>	<i>Allowed (2)</i> <i>Prohibited (1)</i>	<i>Allowed without annotations. (1)</i> <i>Allowed provided that the glycerine used in the production of glycerol monooleate must be made by hydrolysis of fats and oils. (1)</i> <i>Prohibited without annotations. (1)</i>

¹ This Technical Advisory Panel (TAP) review is based on the information available as of the date of this review. This review addresses the requirements of the Organic Foods Production Act to the best of the investigator's ability, and has been reviewed by experts on the TAP. The substance is evaluated against the criteria found in section 2119(m) of the OFPA [7 USC 6517(m)]. The information and advice presented to the NOSB is based on the technical evaluation against that criteria, and does not incorporate commercial availability, socio-economic impact or other factors that the NOSB and the USDA may want to consider in making decisions.

Characterization

Composition: Empirical: $C_{21}H_{40}O_4$

Formula: $CH_3(CH_2)_7CH = CH(CH_2)_7COOCH_2CCH_2OH$

Properties: Glycerol monooleate is a clear amber or pale yellow liquid (Magrabar, 1997; Uniqema, 1999). It is insoluble in water, very slightly soluble in cold alcohol, and soluble in hot alcohol, in chloroform, in ether, and in petroleum ether (Food Chemicals Codex, 1996). Glycerol monooleate is also oil soluble, giving it particularly desirable properties as a food emulsion (Chen and Dickinson, 1999). Like other surfactants, its properties are distinct from those of the reactants. Glycerol monooleate can form a micro-emulsion in water. Glycerine is completely soluble in water, while oleic acid is insoluble in water (Burdock, 1997). The hydrophilic-lipophilic balance (HLB) of glycerol monooleate is 3.8 (Griffin, 1979).

How Made: The processes described here are based on published literature. Information on the manufacturing processes for the listed sources in the petition was not able to be obtained.

Glycerol monooleate is prepared by esterifying glycerin with food-grade oleic acid in the presence of a suitable catalyst to form a monoglyceride ester (Food Chemicals Codex, 1996; Burdock, 1997). Glycerol Monooleate (GM) is a synthetic surface-active chemical widely used as a nonionic surfactant and emulsant. It is produced by the reaction of glycerine and oleic acid over a catalyst to form a monoglyceride ester (Burdock, 1997). Both batch and continuous synthesis routes are used (Sanchez et. al., 1997; Lauridsen, 1976). Commercial production of monoglycerides is described in detail by Gupta (1996):

“Monoglycerides are made by reacting triglycerides with excess glycerol in presence of a catalyst” (glycerolysis reaction, which is a transesterification). The finished product generally contains 35-50% monoglycerides, hence the Food Chemicals Codex requirement of “not less than 35% monoglycerides.” “The rest consists of diglycerides, some unreacted triglycerides, residual glycerol, and free fatty acids.” “It should be pointed out that the free fatty acid is not true fatty acid, but titratable acid. Phosphoric acid, added in slight excess at the neutralization step, leaves some residue in the product along with the (fatty) acid salts.”

The basic ingredients for commercial production of monoglycerides are: partially or fully hydrogenated deodorized vegetable oils, glycerol, and sodium hydroxide as a catalyst. Catalysts can also be Sn^{++} , Zn^{++} , sodium glyceroxide or other metal glyceroxides. When NaOH is used as a catalyst, phosphoric acid is later added for neutralization (Gupta, 1996).

Glycerin is obtained from fats or oils as a by-product of the production of soaps and fatty acids (Budavari, 1996). Glycerin can also be produced by fermentation of sugars and synthesized from propylene (Burdock 1997). Saponification involves the reaction of a fat or oil with potassium hydroxide or another alkali solution (Streitweiser and Heathcock, 1985). Recovery usually involves aluminum sulfate, sulfuric acid, or hydrochloric acid (Jungermann, 1979). Glycerin can be purified by ion exchange (Helfferich, 1962). Glycerin is on the National List of allowed synthetics at 7 CFR 205.605(b)(13): produced by hydrolysis of fats and oils.

Glycerin can also be prepared from a number of petrochemical sources by a variety of processes (Foster, 1986). Early efforts to synthesize glycerin from fermentation sources involved acetaldehyde and sodium sulfite (Budavari, 1996). Other fermentation methods have been developed since that time. The first entirely synthetic source of glycerin resulted from the large stream of products from the chlorination of propylene glycol to produce allyl chloride (Groll, et al, 1938). One method uses chlorohydrination of allyl chloride to produce a mixture of epichlorohydrin and dichlorohydrin. Dichlorohydrin can be hydrolyzed to produce glycerin (Foster, 1986).

Oleic acid is usually obtained by hydrolysis of fats or oils (Budavari, 1996). Oleic acid is generally either extracted from natural fats or from tall oil, itself a pine sap derivative (Burdock, 1997). The source of fats can be vegetable or animal. The primary vegetable oils used to manufacture oleic acid include soybean, cottonseed, corn, and canola. Genetically modified varieties of each of these plants have been commercially released. Oleic acid can also be synthesized (Budavari, 1996) and recovered from tall (pine) oil resulting from pulp and paper manufacture (Formo, 1982). It is possible to enzymatically split fats using various lipolytic enzymes, although this is usually limited to sensitive fats and oils (Sonntag, 1982). These are commercially available from a wide range of non-GMO sources. For example, triacylglycerol lipase from fungal, bacterial, animal, or plant sources (White and White, 1997). Solvents involved may be methanol, ethanol, isopropanol, or acetone (Myers and Muckerheide, 1942; Myers and Muckerheide, 1947; Formo, 1982).

Some glycerol esters are prepared by reaction with epoxides such as ethylene oxide and propylene oxide (Simons, 1983). This review generally does not include the products of such a reaction, but some of the general references do not distinguish glycerol esters based on the method of preparation.

Specific Uses: It is used as an antifoam in juice processing and as a lipophilic emulsifier for water-in-oil applications. It also serves as a moisturizer, emulsifier, and flavoring agent. Various forms of glycerol oleate are widely used in cosmetics (Cosmetic Ingredient Review Expert Panel, 1986). It is also widely used as an excipient in antibiotics and other drugs.

The petition addresses the specific use as a defoaming agent. The petition states, "There is the potential for foam to be discharged up the exhaust line and to the roof" (Ellertson, 2001).

The petition states, "Flash boiling causes foaming and is one of the stages where anti-foam is critical. If air (in the form of foaming) enters the system, it causes many problems. One of the most difficult to deal with is the issue of under weight containers. If there is air in the system it does not allow the fillers to put the legal weight of liquid into the container. A second critical function of the anti-foam is the prevention of product loss from boil over in the vacuum chamber.

"After the vacuum chamber, the milk goes to final cooling, is transferred to a sterilized tank, and then sent to a filler. These transfers, via pumps and valves, are further causes of air incorporating into the product. The fillers do have anti-foaming devices on them. An example would be mesh screens that all products must pass through just before going into the milk carton. Mechanical anti-foaming devices such as these do not provide sufficient anti-foam protection in products susceptible to foaming. Susceptible products include lowfat and nonfat milk products, which inherently have more severe foaming problems due to the reduced fat level. Fat has anti-foam properties.

"In aseptic milk there is an additional step that causes foam. As milk is going into the filler, the milk cartons are simultaneously being formed into shape and readied for the milk (in a sterile environment). At that point, as the milk is filling the packages, nitrogen is injected in to displace oxygen. Without this step, the milk would oxidize over time, and develop severe flavor defects. This nitrogen addition causes foaming in no-fat and low fat milk products affecting the ability to fill to legal weight. Additionally, excess foaming adversely affects the ability of the package to properly seal. . . .

"[Pineapple and carrot juices] tend to foam excessively during blending. If anti-foam is not used, excess air from foaming will insulate the product and prevent adequate heat transfer for pasteurization. By using anti-foam, air incorporated during blending is released, and therefore all particles are fully pasteurized, in keeping with Federal Regulations" (Shea, 2001).

The petition states, "During the harvest and processing, Spirulina and its media are pumped into the harvest building and concentrated by washing onto sequentially finer stainless steel screens. The media is pumped at approximately 800 gallons per minute which results in a great deal of foaming due to the tremendous flow rates and turbulence caused by the screening. An antifoam agent is necessary during this processing stage otherwise the algae foams, will not harvest properly, and most of the product is subsequently wasted" (Cyanotech, 2001).

Containment and inhibition of foam is necessary in food processing for efficient operation of production equipment, to reduce product waste, to maintain a safe workplace, and to keep facilities clean and sanitary (Kouloheris, 1974; Bryon, 1990; Combs, 2000).

Action: The surface tension and solubility in oil or water of the anti-foaming agent is based on the hydrophilic ('water-loving') / lipophilic ('oil-loving') nature of a surface-active agent and is denoted by the HLB (hydrophilic-lipophilic balance) number. Surface-active agents with low HLB (2 - 8) are oil-soluble, while those with high HLB (14 - 18) are water-soluble (Griffin & Lynch, 1968). Glycerol monooleate is lipophilic and binds to fatty parts of a liquid. It is a surface-active agent (surfactant) that breaks the tension of a foam bubble.

Combinations: In juice production, glycerol monooleate is mixed with water (Ellertson, 2001). Milk ultrapasteurization (UP) systems may also involve the use of ammonium hydroxide as a boiler water additive (Muncie, 2001). Commercial formulations may contain butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), citric acid, polymeric dyes, propyl gallate, propylene glycol, sorbitan monostearate, tertiary butylated hydroquinone (TBHQ), and various vegetable oils (Ash and Ash, 1995; Furia, 1980; Ockerman, 1991).

Status

Historic Use: The addition of fatty acid esters to improve the processing of dehydrated and reconstituted fruit and vegetable juices was patented in 1951 (Strashun).

OFPA, USDA Final Rule:

Glycerol monooleate is a monoglyceride. Mono- and di-glycerides are allowed for use in drum drying of food [7 CFR 205.605(b)(12)]. Otherwise, glycerol monooleate does not specifically appear on the National List of Allowed Non-organic ingredients (7 CFR 205.605).

Regulatory: FDA approved uses are covered in Table 1.

Table 1: FDA References to Glyceryl Monooleate	
21 CFR	Section Title
175.300	Resinous and polymeric coatings.
175.320	Resinous and polymeric coatings for polyolefin films.
181.27	Specific Prior-Sanctioned Food Ingredients--Plasticizers.
184.1323	Direct food substances affirmed as generally recognized as safe--Glyceryl monooleate.
Source: EAFUS	

EPA/NIEHS/Other Sources

EPA – List 4 inert ingredient.

NIEHS – Not listed in the National Toxicology Program (NTP) database.

Other Sources – OSHA status: non-hazardous. NTP Cancer classification: not classified.

Status Among U.S. Certifiers

Not able to find it in any standards or generic lists. The petition states one certifier allows it (Ellertson, Shea and Lorenz, 2001).

International

CODEX – Not listed.

EU 2092/91 – Not listed.

IFOAM – Not listed.

Canada – Not listed.

Japanese Agricultural Standard – Not listed.

Section 2119 OFPA U.S.C. 6518(m)(1-7) Criteria

1. *The potential of the substance for detrimental chemical interactions with other materials used in organic farming systems.*

The material is used in processing and is not likely to be released in organic farming systems.

2. *The toxicity and mode of action of the substance and of its breakdown products or any contaminants, and their persistence and areas of concentration in the environment.*

The substance is edible and is not released into the environment.

3. *The probability of environmental contamination during manufacture, use, misuse, or disposal of the substance.*

This is addressed in Processing Criteria #2 below.

4. *The effects of the substance on human health.*

This is addressed in Processing Criteria #3 below.

5. *The effects of the substance on biological and chemical interactions in the agroecosystem, including the physiological effects of the substance on soil organisms (including the salt index and solubility of the soil), crops and livestock.*

When used as petitioned, it is not applied to and does not substantially interact with the agroecosystem.

6. *The alternatives to using the substance in terms of practices or other available materials.*

See Processing Criteria #1 and #7 below.

7. *Its compatibility with a system of sustainable agriculture.*

See Processing Criteria #6, below.

Criteria From the February 10, 1999 NOSB Meeting

A PROCESSING AID OR ADJUVANT may be used if:

1. *It cannot be produced from a natural source and has no organic ingredients as substitutes.*

While it theoretically can be produced from a natural and organic source, all commercial sources are non-organic and synthetic. Based on the description by Gupta in "Bailey's Industrial Oil and Fats Products" (1996), the product would

be considered as a synthetic non-agricultural substance by the NOP (Federal Register, Vol. 65, No. 246, page 80638-80639, subpart A, §205.2).

A search in the US Patent database (www.uspto.gov) did not yield any recent manufacturing or extraction process for glycerol monooleate or monoolein.

A review of all 5 volumes of "Bailey's Industrial Oil and Fats Products" (1996) revealed that manufacturing of other glyceryl esters also involves transesterification as well as fatty acid hydrogenation (example glyceryl monostearate).

2. *Its manufacture, use, and disposal do not have adverse effects on the environment and are done in a manner compatible with organic handling as described in section 6513 of the OFPA.*

If the glycerin is derived from animal or plant fats that are not GMO sources, rather than from petrochemical sources, then the manufacturing process does not entail any of the environmental concerns associated with petroleum refining or genetic engineering. As described in Gupta (1996), commercial production of glyceryl monoesters is a batch process. Purification involves either molecular distillation, or different reaction temperatures and reactant ratios. Theoretically, synthesis that involves the condensation of a carboxylic acid with an alcohol usually produces water as its only waste product (Tau, Elango, and McDonough, 1994). However, as described above in the 'How Made' section, glycerol monooleate manufacture is a transesterification, i.e., a transfer of one or more acyl groups from one ester to another alcohol (glycerol). The process involves reactions with acids and bases in addition to oleic acid and glycerin. Excess glycerol from the process is recovered and reused (Gupta, 1996). Non-volatile esters, such as oleates, may involve the use of toluene to remove the azeotrope from the reaction mixture (Simons, 1983).

3. *If the nutritional quality of the food is maintained and the material itself or its breakdown products do not have adverse effects on human health as defined by applicable Federal regulations.*

Several sources refer to either glycerol oleate (Cosmetic Ingredient Review Expert Panel, 1986; Ash and Ash, 1995) or to the constituent moieties (Hine et al., 1953; Winter, 1989). More recent research based on more advanced toxicology methods and a review of the pharmacological literature suggests that there may be some additional health concerns not detected in the earlier studies (see Reviewer 3's comments below). None of the studies that appear in the references indicated that the nutritional quality of the food is impaired by the use of the substance. Various glycerol oleates are readily digested and metabolized (Cosmetic Ingredient Review Expert Panel, 1986).

When used according to Good Manufacturing Practices, the substance does not have any apparent adverse effect as defined by the applicable Federal regulations. A lengthy review of the toxicology literature found no evidence of oncogenicity (Cosmetic Ingredient Review Expert Panel, 1986). There is some evidence that glycerol monooleate may inhibit carcinogenesis and tumor growth (Cosmetic Ingredient Review Expert Panel, 1986; Longnecker, et al., 1987). However, oleic acid by itself may be oncogenic (Winter, 1989).

Glycerol monooleate is a skin and eye irritant that emits acrid smoke and irritating fumes when heated to decomposition (Lewis, 2000). Animal data show that high levels of GM could cause some eye irritation in rabbits and equivocal tumor initiation in rats (Cosmetic Ingredient Review Expert Group, 1986). This report, however, shows that exposure to or ingestion of GM amounts in food products do not appear to be harmful to humans. The health and safety risks of defoamers are comparable to the risks posed by foam (Owen, 1994). The relative risk depends on the nature of the process, the food, and the foam-producing substance.

4. *Its primary purpose is not as a preservative or used only to recreate/improve flavors, colors, textures, or nutritive value lost during processing except in the latter case as required by law.*

The primary purpose petitioned is as an antifoaming agent. Glycerol monooleate may be used as a flavoring agent or as a moisturizer (Ash and Ash, 1995). Glyceryl esters are antimicrobial in certain circumstances (Lindsay, 1996). These other applications are not considered in this review.

5. *Is Generally Recognized As Safe (GRAS) by FDA when used in accordance with Good Manufacturing Practices (GMP), and contains no residues of heavy metals or other contaminants in excess of FDA tolerances.*

Glyceryl monooleate is listed as GRAS by FDA (21 CFR 184.1323) with no limitations for the functions and food groups listed in Table 2. Monoglycerides are also GRAS (21 CFR 184.1505). As a monoglyceride, glycerol monooleate would not have a limiting maximum daily acceptable human intake limit set by the Joint FAO/WHO Expert Committee on Food Additives (Lauridsen, 1976).

<p>Table 2 FDA GRAS Uses of Glyceryl Monooleate</p>

21 CFR	Function / Food Group
170.3(o)(12)	flavoring agent and adjuvant
170.3(o)(27)	solvent and vehicle
170.3(n)(1)	baked goods and baking mixes
170.3(n)(3)	nonalcoholic beverages and beverage bases
170.3(n)(6)	chewing gum
170.3(n)(29)	meat products
Source: 21 CFR 184.1323	

From the Food Chemicals Codex (1996):

Assay: Not less than 35.0% monoglycerides, calculated on an anhydrous basis.

Acid value: Not more than 6

Free Glycerin: Not more than 6.0%.

Heavy Metals: Not more than 10 mg/kg

Hydroxyl value: Between 300 and 330.

Iodine value: Between 58 and 80

Lead: Not more than 1 mg/kg

Residue on ignition: Not more than 0.1%

Saponification value¹: Between 160 and 176 Water: Not more than 1.0%

6. *Its use is compatible with the principles of organic handling*

Compatibility depends on the source, manufacturing process, and specific use. Glycerin from petroleum sources would not be compatible, based on the NOSB's previous recommendation. Fats or oils used to make the glycerin or the oleic acid would have to be obtained from sources that are not genetically modified organisms.

The process of esterification may involve the use of certain solvents that have been prohibited for use with certified organic edible oils. Glycerol monooleate resolved with toluene may be considered acceptable in products that make a 'made with organic [specific ingredients]' claim, but would not be acceptable for use with non-organic ingredients with the same standard that has been applied to oils in the NOP Final Rule [7 CFR 205.270(c)(2)]. This standard is also applied to certain specific non-organic ingredients, such as natural flavors [7 CFR 205.605(a)(9)]. Use as a flavoring agent or to improve texture would also not be considered compatible with organic production (see Processing Criteria #4 above).

Given the safety concerns regarding foam, it is difficult to say that such an application would be incompatible. However, the petition did not indicate a specific need for glycerol monooleate or explain why physical, mechanical, organic, and listed non-organic methods were not acceptable.

7. *There is no other way to produce a similar product without its use and it is used in the minimum quantity required to achieve the process.*

From the petition: Levels of addition to juice in production ranges from 10-40 ppm antifoam (Ellertson, 2001). For milk, the anti-foam does not exceed 0.03% by weight (Shea, 2001).

Mechanical and physical methods can be used to avoid foam, but chemical defoamers are generally more effective and economical than mechanical or physical methods (Kouloheris, 1974; Zotto, 1991; Combs, 2000). Non-chemical means include heating, centrifuging, spraying, or ultrasonic vibrations (Combs, 2000). One organic food processor has opted to install mechanical and physical defoaming equipment to avoid the contamination problems posed by chemical defoamers (Sequeira, 2001). Defoamerless fluid processing equipment is available and has been installed in some processing facilities (Elliot, 1989). For example, bottom-up filling of milk cartons avoids the creation of air bubbles from dropping the fluid. Rotating blades and paddles knock down and break foam. Spray jets and vacuums use pressure differentials to burst bubbles. Ultrasound can use sonic waves to break the bubbles that form foam by rapid local change in the elasticity. Such devices have been installed by pharmaceutical companies and food processors that found it necessary to avoid contamination by chemical antifoaming agents (Kouloheris, 1974).

Naturally occurring substances and agricultural products can be used as defoaming agents. The use of fats and oils to reduce foams has long been understood (Bryon, 1990; Garrett, 1993; Owen, 1994). In addition to organic vegetable oils, a number of substances already on the National List can be used for defoaming. Whether or not these produce a similar product is not addressed in the petition or this review.

¹ Number of milligrams of KOH needed to neutralize the free acids and turn one gram of the test sample into soap.

The effectiveness of a given defoaming agent depends on: the chemical nature and foaming tendency of the foam-forming food; solubility and concentration of the defoamer; the presence of electrolytes, colloids, or other surface-active agents; temperature, pH, and viscosity; processing equipment; and end-use of the food product (Zotto, 1991). Both the nature of foam (see, for example, Hawks, et al, 1993) and the nature of emulsifiers (see Johansson and Bergenstahl, 1992; and Chen and Dickinson, 1999) are highly variable.

Silicon dioxide is approved as a defoaming agent under 21 CFR 173.340(a)(2). Substances that are GRAS or are approved by prior sanction may also be used as defoamers [21 CFR 173.340(a)(1)]. Glycerin and lecithin would fall into this category. Glycerin is the alcohol moiety of the petitioned substance. Lecithin is a mixture of diglycerides of fatty acids linked to the choline ester of phosphoric acid. When lecithin is combined with a non-silicone amorphous silica it can defoam liquids such as blood, milk, beer, and soda (Friedman, 2001). Liquid monoglycerides can also be used as a defoamer (Furia, 1972) and are currently limited under the National Organic Program to drum drying of food [7 CFR 205.605(b)(12)].

TAP Reviewer Discussion²

Reviewer 1 [research chemist who serves on an organic certification committee]

... Glycerol Monooleate and its precursors are not harmful to the environment. All three materials occur in natural animal and plant fats. Oleic acid is extracted from natural product. Glycerine can be made from natural fats or petrochemicals. Glycerine appears on the National List of allowed synthetic materials for processing with the annotation "produced by hydrolysis of fats and oils" (7 CFR 205.605.b.12). A similar annotation could be added to glycerol monooleate, if the material were to be added to the National List. Glycerine produced from propane usually has the CAS # 115-07-1 instead of the more general # 56-81-5 (Jakobson et al., 1985).

Glycerol monooleate is a food processing aid that would only be used in large integrated plants. It should not have any interactions with the agroecosystem. An exception would be filtered juice solids, which are landfilled or later sold as a livestock food supplement. The material is edible and does not appear to be harmful to humans at the concentrations used in food processing.

Natural oils, glycerine, lecithin, or lanolin have also been used as surface-active agents and antifoamers. Silicon dioxide (SiO₂)—usually synthetic fumed silica—is also an antifoaming agent when suspended in an appropriate surfactant (Fordham, 1961). Natural oils are a mixture of triglycerides and free fatty acids. Natural oils commonly used as surface-active agents are castor, corn, cottonseed, linseed, olive, sesame, soybean, sunflower, and tall oil (Vardar-Sukan, 1998; Mayhew and Ottley 1961, Steiner et. al. 1960). Natural oils are insoluble in water and can impart a flavor to the finished product. The poor dispensability of natural oil in water emulsions (o / w) based systems limits their usefulness as antifoaming agents. Surfactants are commonly added to increase their dispensability because good dispersion is needed to get the antifoaming agent into the liquid between the foam bubbles (Vardar-Sukan, 1998; Mayhew and Ottley 1961). Fatty acid esters (HLB ~ 17, or polyoxyethylates (HLB 18) can greatly increase the ability of the oil to knock down foams (Mayhew & Ottley 1961).

Lanolin (HLB 17) and soya lecithin (HLB 8.0) are surface-active agents that could act as antifoamers for different products. Polyoxyethylene (HLB 15) is extensively used as an antifoamer in sugar processing, but would not be the best antifoamer in fruit juice processing (Griffin & Lynch, 1968).

Access to a short list of GRAS and environmentally benign surface-active agents would be useful to organic food processors. The hydrophilic/lipophilic nature of the agents is not the only important property of these agents in food systems. [However, the HLB] affects foaming through the emulsion behavior and the phase partitioning of the agent in food oil/water systems for antifoaming, the surface-active agent should partition into the foam, more than the bulk liquid. A possible list of surface-active agents might include compounds like a low HLB fatty acid (Oleic), a mono- or di-glyceride such as glycerol monooleate, soya lecithin, and a high HLB agent such as a lanolin or fatty acid ester.

[Reviewer 1] Conclusion

Glycerol monooleate is a synthetic material that should be added to the National List of Allowed Non-organic Ingredients. The following annotation should be included: Glycerine used in the production of glycerol monooleate must be produced by hydrolysis of fats and oils. This annotation would prevent the use of glycerine made from petrochemicals or produced by genetically modified microbes in the manufacture of glycerol monooleate.

² OMRI's information is enclosed in square brackets in italics. Where a reviewer corrected a technical point (e.g., the word should be "intravenous" rather than "subcutaneous"), these corrections were made in this document and are not listed here in the Reviewer Comments. The rest of the TAP Reviewer's comments are edited for any identifying comments, redundant statements, and typographical errors. Text removed is identified by ellipses [...]. Statements expressed by reviewers are their own and do not reflect the opinions of any other individual or organizations.

Reviewer 2 [food scientist who has performed organic food processing inspections]

... It is theoretically possible for it to be produced from natural sources, but [this reviewer does not know] whether production from these sources is practical. . . The known natural sources would seem to offer the potential for it to be produced from organic sources. . . [The] reviewer [does not know] whether the production processes necessary to extract it from these potential organic sources would retain its organic or even its agricultural product status.

The petitioners have not shown data (or even made statements) indicating that silicon dioxide or mechanical means are unsuitable defoamers in their products. They have also not indicated why natural sources of glycerol monooleate are not being used. Since there are potentially natural sources of the material, which would not need to be petitioned (unless the process of extraction or purification might be prohibited), I see little reason to approve this synthetic source of the material. . .

Its use in 'made with organic' products would be acceptable.

Reviewer 3 [food chemist with experience as an organic food processing inspector]

One difficulty with "Glyceryl monooleate" is that it is an ill-defined product, and contains more than the monoacylglyceride:

- 21 CFR 184.1323 (a): "... It contains glyceryl monooleate and glyceryl esters of fatty acids present in commercial oleic acids."
- 21 CFR 184.1323 (b): "FDA is developing food-grade specifications for glyceryl monooleate in cooperation with the National Academy of Sciences."
- The Food Chemical Codex mentions "no less than 35% monoglycerides."
- In typical operations, monoglycerides content of the final product are 35% with 46-48% diglycerides and 17-19% triglycerides, or 50% monoglycerides with 40-41% diglycerides and 8-10% triglycerides (Gupta, 1996). Additionally, there is residual phosphoric acid along with fatty acid salts.
- The technical sheet provided by one of the manufacturers in the petition says "monoglycerides %: 40.0 to 180.0." The fact that the percent may be more than 100, and the range from 40 to 180 percent, may imply that there are undisclosed other "inert" ingredient(s) in that specific commercial glycerol monooleate.

Diacylglycerol (i.e., diglyceride), the second most prevalent component of "glycerol monooleate," is an important intermediate in cell signaling pathways that use plasma membrane receptors linked to G-proteins (Alberts et al., 1994). Those pathways are involved in cell proliferation and growth, as well as many other cellular functions. In these pathways, diacylglycerol activates a crucial serine/threonine protein kinase, C-kinase, which phosphorylates selected proteins in target cells. It has been shown that the activation of C-kinase increases the transcription of specific genes involved in cellular proliferation as well as numerous other genes (Alberts et al., 1994).

High levels of diacylglycerol were found in malignant prostatic tissue in comparison to benign tissue (Chaudry et al., 1994). High levels of fecal diacylglycerol were shown to stimulate epithelial cell proliferation (Holt et al., 1996; Atillasoy et al., 1995). In those studies, the elevated diacylglycerol in proliferative tissue was a result of high dietary fat intake. In another study, one group of the mice fed diacylglycerol oil developed benign or malignant mammary gland neoplasms (Soni et al., 2001). In spite of this result showing tumorigenesis in one group of the subjects, the authors conclude that there is no toxicologically significant effect of diacylglycerol oil consumption. The full text article was not available to this reviewer at this time to perhaps elucidate the apparent contradiction. The same authors (Soni et al., 2001) say that some unspecified level of diacylglycerol has been approved for use in cooking oil in Japan. Regardless of the possible toxicity of diacylglycerol, there are several published examples of the biological activity of dietary diacylglycerol. Several Japanese authors studied the effect of dietary diacylglycerol in suppressing fat accumulation in tissue (Taguchi et al., 2000; Murase et al. 2001).

With . . . [specific reference to] glycerol monooleate, a search in *Toxline* revealed at least six studies (out of 33) where glyceryl monooleate enhances drug bioavailability by enhancing absorption through the large intestine (Maderich and Sugita, 1996; Hastewell et al., 1994; Charman et al., 1993; Muranushi et al., 1980; Okada et al., 1982; Ogiso et al., 1995), and through the mouth mucosa (Engstrom et al., 1995).

The positive results for the Ehrlich ascites tumor assay as described in the Cosmetic Ingredient Review Expert Panel (1986), provides the only suggestion that glycerol oleate may inhibit experimental tumors. However, this also implies that glyceryl monooleate may enhance immune surveillance, and therefore may increase the severity of allergies and affect patients suffering from auto-immune diseases (B.L. Ford, PhD toxicology, personal communication).

In reference to the statement in [NOSB Criteria 3]: “Various glycerol oleates are readily digested and metabolized (Cosmetic Ingredient Review Expert Panel, 1986)”: Digestion and metabolism of potential toxins does not necessarily mean they are non-toxic. In fact, many toxins require metabolic activation to become toxic after digestion (Parkinson, 1996).

[Reviewer 3] Summary:

Glyceryl monooleate is not biologically “inert” since it can be used pharmaceutically to enhance drug absorption (Maderich and Sugita, 1996; Hastewell et al., 1994; Charman et al., 1993; Muranushi et al., 1980; Okada et al., 1982; Ogiso et al., 1995; Engstrom et al., 1995).

Glyceryl monooleate is not a pure substance (21 CFR 184.1323; Gupta, 1996). It contains diacylglycerol, which itself is involved in many cellular processes, including signaling cell growth and proliferation (Alberts et al., 1994). Diacylglycerol was shown to be involved in tumorigenesis (Holt et al., 1996; Atillasoy et al., 1995) and decrease fat accumulation in tissue (Taguchi et al., 2000; Murase et al. 2001).

“Glycerol monooleate” is manufactured from synthetically hydrogenated fats (Gupta, 1996) and would therefore contain a substantial amount of the unnatural *trans*-isomer of oleic acid. Furthermore, the use of strong catalysts in the process such as NaOH with further addition of phosphoric acid is likely not compatible with NOSB criteria.

Alternatives to chemical defoamers include physical or mechanical methods, and documents were provided to the reviewers showing it is being done industrially. Additionally, this reviewer has never encountered any addition of any chemical defoamer to juice processing or milk packaging in organic processes. Therefore, a chemical defoamer such as glycerol monooleate does not seem to be “vital” (i.e., there is no safety hazard due to foam, the product can be made without it) to the process of fruit juice processing or milk packaging.

While there is insufficient information provided on the commercial product that is being petitioned, this review was done based on published data, and may not reflect the possibility of the manufacture of a natural defoamer that would conform to the organic standards. As it stands, the product being petitioned fails to meet organic standards.

If the substance were >99% glycerol *α*-monooleate, and if it were manufactured in a manner compatible with organic handling, the reviewer feels that it might be added to the National List of Allowed Non-Organic Ingredients as a processing aid. If allowed, there should be restrictions as to the amount used, and to which commodities. Because glycerol monooleate is insoluble in water, its use as antifoam in fruit juices at levels less than 50 ppm (as stated in the petition) prior to filtration would probably result in trace amounts in the final product (this would need to be substantiated with independent laboratory analysis). On the other hand, because it is fat-soluble, glycerol monooleate should not be allowed in dairy and other fat-containing products.

The TAP Reviewers were also asked the following questions:

Similar questions were posted to the OMRI web site.

1) Processing Criteria #1: Is glycerol monooleate always synthetic, can it be made from natural and from synthetic sources, or is it always nonsynthetic?

All reviewers considered all commercial sources to be synthetic.

Reviewer 1: Although the glycerine and oleic acid intermediates can be derived from natural sources, glycerol monooleate is a product of a synthetic chemical reaction.

Reviewer 2: In this petition it would be considered synthetic because of the processes listed to produce it. It can be made from natural sources as discussed in 2 below.

Reviewer 3: The *Bailey's Industrial Oil and Fat Products* appears to be a reference for the oil industry and details the commercial production of monoglycerides. From this reference and a search in the patent database, I do not have the impression that glycerol monooleate can be extracted in high purity from a natural source, without involving processes that would make it synthetic.

2) Glycerol monooleate is naturally occurring in tallow and cocoa butter (Food Chemicals Codex, 1996). Can it be extracted and then used? If it is natural, is it possible to make it from organic sources? Should glycerol monooleate be considered an agricultural product that is subject to commercial availability requirements?

Reviewer 1: Commercially produced Glycerol Monooleate is a synthetic chemical.

Reviewer 2: It could be extracted from these or other natural sources. If the petitioners were proposing to use it from one of these natural sources, then I would consider it an agricultural product with the associated acceptances and allowances (would have to review the extraction and purification procedure to determine if it would be allowed in a 100% product; allowed in a 95% product; allowed in a 'made with organic' product). It might be possible to make it from an organic source (rendering tallow from organic meat or growing organic cocoa), but the process would have to be reviewed, which is beyond the scope of this review.

Reviewer 3: See response to question 1.

3) Processing Criteria #6: Do you know of organic food processors who have installed mechanical and physical defoaming equipment as a way to control foam problems without chemical defoamers?

Reviewer 1: The main question regarding its applicability to organic food processing is whether there are viable nonsynthetic alternatives to prevent foaming. There are two main means to prevent/destroy foams that form in food processing: chemical (antifoaming and defoaming), and mechanical defoaming. A chemical antifoam is a surface active agent that is added in the process stream before foaming becomes a problem. A chemical defoamer is added after a foam is formed. An example of the latter would be a fermentation vat with a sensor (optical or electrical conductivity) placed at a certain height above the top of the liquid. If a foam rises to the height of the sensor, a surfactant is sprayed on the foam to knock it down. Mechanical devices impart mechanical or ultrasonic energy to a foam to break it up. An antifoaming chemical can prevent the formation of foam throughout an entire process. Defoamers (mechanical or chemical) can only act on a foam after it has formed, and can not prevent foam reforming in some later process.

Mechanical defoaming is extensively used in pharmaceutical fermentation processes (Kouloheris, 1974, Vardar-Sukan, 1998). Mechanical methods are used because chemical antifoamers can interfere with microbe growth and product formation (Schlegel et. al., 1985). Mechanical stirrers and impellers can be efficient in certain batch operations but can be very complicated and costly to operate (Vardar-Sukan 1998; Deshpande and Mostafa, 1999). In continuous operations, injectors and orifices (which cause sudden pressure drops) must be employed. Simple mechanical defoaming is difficult to achieve, and most authors recommend a combination of mechanical and chemical means (Vardar-Sukan, 1998; Kouloheris, 1974).

Mechanical defoaming in a continuous process with many steps could be extremely complicated. Each defoaming process could become a control point that needs maintenance to prevent microbial contamination. . .

Reviewer 2: As listed in the packet at least one organic processor has done this. I have not encountered the use of glycerol monooleate in any of the processors that I have visited. Either other approved defoamers are used (silicon dioxide) or mechanical means have been sufficient to eliminate the problem.

Reviewer 3: I do not know any food processor that has installed a physical defoaming process. However, I have never seen glyceryl monooleate used as a defoamer, in either juice or dairy organic processing.

4) How much of a concern is the fact that both the glycerin and the oleic acid can be derived from GMO sources? From synthetic sources? If it is added to the National List, should there be an annotation that the glycerin be derived from hydrolysis of fats and oils? Is extraction of fats or oils from genetically modified plants considered the product of a genetically modified organism? As a practical matter, how easy is it for certifiers and processors to verify that the sources for [glycerol monooleate] are non-GMO?

Reviewer 1 Both Glycerine and Oleic Acid could be produced from fats derived from GMO sources. In neither case would original GMO protein be carried over to the product, and the materials would be allowed by the OMRI decision tree step 4H. Since Glycerine could also be produced by fermentation, GMO microbes could directly make the Glycerine. The annotation "produced by hydrolysis of fats and oils" could be used to prevent any GMO derived Glycerine or Glycerine products from entering Organic products.

Reviewer 2: GMO sources of materials are always a concern, as are synthetic sources, when there is also a natural source. This requires extra diligence and checks on the part of the manufacturer to insure only acceptable sources are used. If it is added, the annotation above should be included if the general wording within the NOP is not sufficient to insure this. The OMRI flow chart would be applicable. I suspect that it would be quite difficult for certifiers to verify that sources are non-GMO...

Reviewer 3: The NOP clearly specifies that the excluded methods (i.e., GMO) also apply to the 5% of non-organic ingredients in products labeled “organic”, and to the 30% of non-organic ingredients in products “made with organic ingredients”. In the case of glyceryl monooleate, the relationship between the ingredients and the final product is quite straightforward. The annotation that glycerin should be derived from hydrolysis of fats and oils also applies here. The extraction of fats or oils from genetically modified plants IS considered the product of a genetically modified organism.

5) Processing Criteria #7:

- a) What are minimum quantities needed to achieve anti-foaming? The quantities listed are from the petition.
- b) Is there any other information regarding Good Manufacturing Practices that needs to be considered by the NOSB in evaluating compatibility?

Reviewer 1: Oil based antifoamers are usually added to food in concentrations between 0.1 and 0.5 wt % (Vardar-Sukan, 1998; Griffin & Lynch, 1968). . . Chemical antifoaming agents must be selected for the specific product being processed. Foaming results from complex chemical and physical processes in the product. The nature of the emulsion, pH of the aqueous phase, temperature, and many other factors determine the antifoaming chemical to be used (Ghildyal et. al., 1988). The antifoam agent must not interact with or impart a color or odor to the final product (Vardar-Sukan, 1998).

Glycerol Monooleate (HLB 3.8) is not readily soluble in water (Cosmetic Science & Technology, 2001). However, it forms very stable o/w emulsions and is a good defoamer for juices and jams (Griffin & Lynch, 1968). For example, the similar surface-active agent, Glycerine Triooleate, can form stable o/w emulsions alone, while the natural Oleic Acid (HLB 1) needs additional surfactants to stabilize the same emulsions (Kamogawa et. al., 2001).

Reviewer 2: The listed quantities are typical of the necessary application rates to achieve efficacy.

Reviewer 3: a) Since there are physical methods to resolve or avoid foam, and since it is not currently being used by the majority of organic juice and dairy processors, the minimum quantity should be *zero*.

b) The glycerol monooleate should be at least 90% monoglyceride (the Gupta reference indicates some processes that can lead to that purity level) and from non-hydrogenated oleic acid. [*emphasis the reviewer's*].

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*Note: * = included in packet*

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- This TAP review was completed pursuant to United States Department of Agriculture Purchase Order 40-6395-0-2900.